cost-effective. At least one previous study has suggested such an economic benefit with the use of nurse practitioners.[5] Whether it indeed was the case in the MASTERPLAN study, however, is unclear. Patients randomized to intensive care had significantly more visits to the health-care facility (7.2 vs. 4.7); however, there were significantly fewer visits to a nephrologist (2.8 vs. 3.7).[3] It is imperative that future studies incorporate cost-effectiveness analyses to evaluate care models using nurse practitioners more comprehensively. Alternatively, nurse practitioner care could be valuable if they focused on aspects of care different from those dealt with by nephrologists and/or if their mandate were more limited than what was attempted in the MASTERPLAN study. Physician visits are often rushed without insufficient time to fully address each aspect of care, and nurse practitioners could supplement areas where care is beleaguered.

In conclusion, the MASTERPLAN trial is a very important study, and both its successes and its failures will inform decision making for the inevitable development of care models that incorporate physician extenders in the care of the high-risk CKD population. The future success of these care models depends on our ability to develop high-level evidence to correctly identify risk factors to be targeted to mitigate cardiovascular risk and disease progression, determine the correct division of labor, and ensure that such care is cost-effective.

DISCLOSURE

Anuja Shah is supported by a research grant from Genzyme. Rajnish Mehrotra has received grant support and/or honoraria from Amgen, Baxter Healthcare, DaVita, Mitsubishi, Shire, Takeda, and Vifor.

REFERENCES

1. Coresh J, Selvin E, Stevens LA *et al.* Prevalence of chronic kidney disease in the United States. *JAMA* 2007; **298**: 2038–2047.
2. Keith DS, Nichols GA, Gullion CM *et al.* Longitudinal follow-up and outcomes among a population with chronic kidney disease in a large managed care organization. *Arch Intern Med* 2004; **164**: 659–663.
3. Van Zuilen AD, Bots ML, Dulger A *et al.* Multifactorial intervention with nurse practitioners does not change cardiovascular outcomes in patients with chronic kidney disease. *Kidney Int* 2012; **82**: 710–717.
4. Senior PA, MacNair L, Jindal K. Delivery of multifactorial interventions by nurse and dietitian teams in a community setting to prevent diabetic complications: a quality-improvement report. *Am J Kidney Dis* 2008; **51**: 425–434.
5. Barrett BJ, Garg AX, Goeree R *et al.* A nurse-coordinated model of care versus usual care for stage 3/4 chronic kidney disease in the community: a randomized controlled trial. *Clin J Am Soc Nephrol* 2011; **6**: 1241–1247.
6. Lee W, Campoy S, Smits G *et al.* Effectiveness of a chronic kidney disease clinic in achieving K/DOQI guideline targets at initiation of dialysis: a single-centre experience. *Nephrol Dial Transplant* 2007; **22**: 833–838.
7. Remuzzi G, Benigni A, Remuzzi A. Mechanisms of progression and regression of renal lesions of chronic nephropathies and diabetes. *J Clin Invest* 2006; **116**: 288–296.
8. Baigent C, Landray MJ, Reith C *et al.* The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial. *Lancet* 2011; **377**: 2181–2192.
9. Singh AK, Szczech L, Tang KL *et al.* Correction of anemia with epoetin alfa in chronic kidney disease. *N Engl J Med* 2006; **355**: 2085–2098.

see original article on page 686

The risks of vascular access

Peter G. Blake[1], Robert R. Quinn[2] and Matthew J. Oliver[3]

Fatal vascular access hemorrhage is considered a rare complication of hemodialysis (HD). Ellingson *et al.* indicate otherwise, and their data suggest that it causes 0.4–1.6% of deaths in US HD patients. It is more common with grafts than fistulas, and many victims have had previous access hemorrhages. The widespread presumption that a fistula is the best, and a cuffed catheter the worst, access for HD patients needs reassessment, particularly in older, sicker patients.

Kidney International (2012) **82,** 623–625. doi:10.1038/ki.2012.181

Most nephrologists with any experience of hemodialysis (HD) will have seen cases of severe vascular access hemorrhage requiring urgent surgical intervention, and some will recall fatalities. However, it is likely that most would consider this complication a rare cause of death, and, until now, there has been little in the literature to suggest otherwise. For this reason, the paper by Ellingson *et al.*[1] (this issue) is both surprising and important. The investigators from the Centers for Disease Control and Prevention became involved when a cluster of such deaths was noticed in Maryland, Virginia, and the District of Columbia. A regional investigation identified 88 fatal vascular access hemorrhage (FVAH) deaths over a 6–year period and noted that only a quarter of these cases had been identified on Centers for Medicare and Medicaid Services (CMS) death reports. Across the United States, a startling 1654 deaths were identified from CMS data in the same period, accounting for 0.4% of all HD deaths. However, if the same underestimation had occurred nationwide, the true number of HD deaths due to FVAH might be more than 6000, corresponding to at least 1000 annually or 1.6% of all HD deaths.

The authors then investigated 88 cases in detail and made important observations. A large majority of the bleeds began in the patient's residence and not in the dialysis unit. More than half involved an arteriovenous graft. The mean age of the patients was only 64 years, and only a very small number of cases appear to have been episodes of 'self-harm'. Compared with case controls, the victims were more likely to have had grafts and to be long-term HD patients, and, most

[1]*Division of Nephrology, London Health Sciences Centre and University of Western Ontario, London, Ontario, Canada;* [2]*Division of Nephrology, Foothills Medical Centre and University of Calgary, Calgary, Alberta, Canada and* [3]*Sunnybrook Health Sciences Centre and University of Toronto, Toronto, Ontario, Canada*

Correspondence: *Peter G. Blake, Division of Nephrology, London Health Sciences Centre, 800 Commissioners Road East, London, Ontario N6A 5W9, Canada. E-mail: peter.blake@lhsc.on.ca*

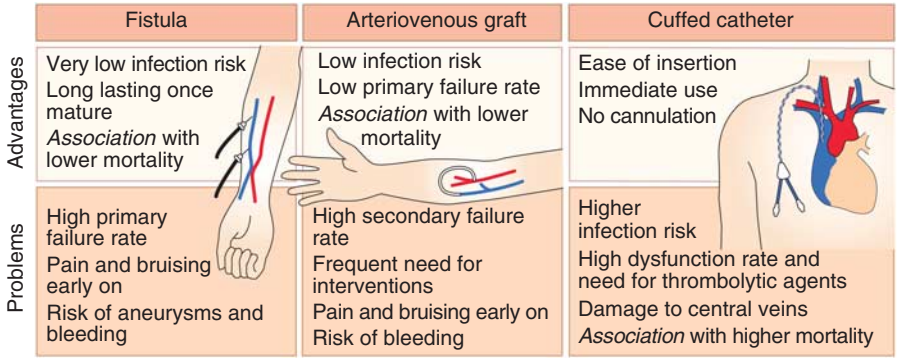

Figure 1 | The advantages and challenges of the major forms of vascular access.

importantly, they were three times more likely to have had an access-related complication within the previous 6 months, usually an infection or a previous bleed. In a subset of cases in which there had been a medical examiner review, 72% had evidence of access erosion, but no information is provided about the presence of aneurysms, which might have been of interest.

What conclusions can be drawn from this important paper? First, FVAH is not a common problem, but we now know it is not rare, and hundreds of patients are dying from it annually in the United States. Second, patients at high risk for FVAH are those who have a graft or fistula that has been infected or has already hemorrhaged, and that may be showing evidence of erosion. Such a situation should now lead to a specific evaluation of the risk of FVAH, and the desirability of ligating the graft or fistula should at least be considered. Survival of the patient is more important than survival of the access. Also, although this complication is rare, HD patients and their families should be regularly educated by HD unit staff on how to deal with acute access hemorrhage.

This leads us to consideration of the broader issue of vascular access in the contemporary HD population. The past decade has seen aggressive efforts to increase the use of fistulas and to reverse the growth in the use of cuffed catheters as a form of definitive access for HD patients.[2,3] This strategy is based on a large volume of circumstantial evidence showing a consistent association between use of cuffed catheters and decreased survival on dialysis relative to what is seen with the use of fistulas.[4–6] The presumed major mechanism is increased infection rates, and, in particular, bacteremia and its complications, in patients with catheters.

There may, however, be the beginning of a reaction to this approach with concern being expressed as to whether fistulas and grafts really are the best access for all patients.[7,8] In this regard, there is some evidence that needs to be noted (Figure 1).

First, failure rates with fistulas are alarmingly high in contemporary populations. In a US multicenter randomized controlled trial on the effect of clopidogrel, more than 60% of 877 fistulas were not adequate for dialysis.[9] In a recent Mayo Clinic study, there was a 37% primary failure and a subsequent 11% secondary failure rate, while 21% of patients had significant postoperative complications.[10] Such failure rates would be unacceptable with most other types of surgery. Second, a sequence of failed fistula construction, repeat attempts that may or may not be successful, difficulty with needling, requirement for salvage procedures, and all the associated pain and inconvenience can be very difficult and unpleasant, especially for patients who may already have an impaired quality of life and multiple comorbidities. All this may not be justifiable in patients with a limited life expectancy.

The alternative approach of using a synthetic graft has a higher success rate and facilitates earlier use but also has a higher and perhaps unacceptable requirement for subsequent interventions and probability of eventual failure.[7] Furthermore, both fistulas and grafts may also be associated with other problems, such as aggravation of cardiac failure; steal syndromes, including overt hand ischemia; pulmonary hypertension; and, as Ellingson *et al.* have now shown, FVAH (Figure 1).[1,8]

Of course, all these risks have to be accepted if those associated with catheter use are clearly greater. Two large US studies have reported that adjusted mortality rates for incident HD patients with catheter access are 1.70 and 1.49, respectively, relative to those with a fistula.[4,5] Moist *et al.* report that incident catheter use in Canada is associated with a remarkable sixfold increase in the mortality rate compared with fistula use.[6] These are observational studies, however, and there is always the reservation that adjustment for baseline comorbidity and other characteristics cannot be complete. In an era in which most North American patients initiate HD via a cuffed catheter, the presence of a functioning fistula is surely a marker of a patient's exceptional health and adherence, and so all or even most of the superior outcome may not be related to the fistula itself. Also, catheter use is inevitably associated with acute illness and late presentation for dialysis, factors that are in turn associated with high mortality and that may be difficult to adjust for. In other words, the association of catheters and mortality may not be causal. Studies have not shown all the excess mortality with catheters to be infection-related, and, in any case, there is evidence that, with increased experience and better preventative strategies, catheter-associated bacteremia rates are falling impressively—to as low as one to two every 3 years in a recent trial.[11]

Notwithstanding all this, a fistula appears to be the access of choice for younger and healthier HD patients. However, for the large number of older, sicker patients with risk factors for fistula failure and associated complications and with shorter life expectancy, the risk-to-benefit ratio changes and it may be reasonable to use a catheter as definitive access. Perhaps it is to time to discard the dogma that has long dominated this area and to propose a randomized controlled trial of fistulas versus cuffed catheters in the high-risk, older, frailer HD population, which is such a prominent feature of North American HD units. Such a trial would look at not only patient survival but also quality of life and degree of pain; access infections and other complications, including

thrombosis and hemorrhage, cardiovascular consequences, and numbers of interventions required; and, not least, cost. The results might be surprising. It would be far from unprecedented for a dogmatic belief about how to care for dialysis patients to be contradicted by a randomized trial.

DISCLOSURE
The authors declared no competing interests.

REFERENCES

1. Ellingson KD, Palekar RS, Lucero CA *et al.* Vascular access hemorrhages contribute to deaths among hemodialysis patients. *Kidney Int* 2012; **82**: 686–692.
2. Vascular Access Work Group. Clinical practice guidelines for vascular access. *Am J Kidney Dis* 2006; **48**(Suppl): S248–S273.
3. *Fistula First National Vascular Access Improvements Initiative*. < http://www.fistulafirst.org > (accessed 5 March 2012).
4. Xue JL, Dahl D, Ebben JP *et al.* The association of initial hemodialysis access type with mortality outcomes in elderly Medicare ESRD patients. *Am J Kidney Dis* 2003; **42**: 1013–1019.
5. Bradbury BD, Fissell RB, Albert JM. Predictors of early mortality among incident US hemodialysis patients in the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Clin J Am Soc Nephrol* 2007; **2**: 89–99.
6. Moist LM, Trpeski L, Na Y *et al.* Increased hemodialysis catheter use in Canada and associated mortality risk: data from the Canadian Organ Replacement Registry 2001-2004. *Clin J Am Soc Nephrol* 2008; **3**: 1726–1732.
7. James MT, Manns BJ, Hemmelgarn BR *et al.* What's next after *Fistula First*: is an arteriovenous graft or central venous catheter preferable when an arteriovenous access is not possible? *Semin Dial* 2009; **22**: 539–544.
8. Amerling R, Ronco C, Kuhlmann M *et al.* Arteriovenous fistula toxicity. *Blood Purif* 2011; **31**: 113–120.
9. Dember LM, Beck GJ, Allon M *et al.* Effect of clopidogrel on early failure of arteriovenous fistulas for hemodialysis. *JAMA* 2008; **299**: 2164–2171.
10. Schinstock CA, Albright RC, Williams AW *et al.* Outcomes of arteriovenous fistula creation after the Fistula First Initiative. *Clin J Am Soc Nephrol* 2011; **6**: 1996–2002.
11. Solomon LR, Cheesborough JS, Ebah L *et al.* A randomized controlled trial of taurioldine-citrate catheter locks for the prevention of bacteremia in patients treated with hemodialysis. *Am J Kidney Dis* 2010; **55**: 1060–1068.

see original article on page 627

The Alternative Iranian model of living renal transplantation

Francis L. Delmonico[1]

The experience of the Iranian model should be carefully considered by those who suggest a pilot trial of a regulated market in organ sales. Mahdavi-Mazdeh's candid report makes clear that a fixed price as the basis of regulation is not possible. Iran is proceeding with an independent program of deceased organ donation in cities such as Shiraz. Mahdavi-Mazdeh's report is encouraging for the prospect of a revitalized expansion of deceased donation.

Kidney International (2012) **82,** 625–626. doi:10.1038/ki.2012.247

Mitra Mahdavi-Mazdeh is a highly regarded physician internationally who represents the best of Iranian medicine. In this issue of *Kidney International*,[1] Dr Mahdavi-Mazdeh presents a candid and comprehensive review of the Iranian model of living renal transplantation. The Iranian living-donor program has spanned two decades, with more than 20,000 vendors participating.[1] Dr Mahdavi-Mazdeh's conclusions are poignant and sobering. The process of identifying an Iranian vendor for a potential kidney transplant recipient ultimately occasions a tense financial bargaining between the donor and the recipient that escapes regulatory control. The vendor wants to be paid more; the recipient wants to pay less. The vendors want more because they are poor; the recipients want to pay less because they may not have the money.

The experience of the Iranian model should be carefully considered by those who suggest a pilot trial of a regulated market in organ sales. This candid report makes clear that a fixed price as the basis of regulation is not possible. The vendor demands more money than is allotted by the government's fixed price, in what Mahdavi-Mazdeh describes as a 'confrontation.' And although the final interaction may be perceived as broker free, the introduction of the recipient to the unrelated donor is not, with shopping at the 137 kidney-foundation outlets throughout the country.

Mahdavi-Mazdeh, like other Iranian colleagues, rationalizes these realities by asserting that the model 'has enabled most of the Iranian kidney transplant candidates, irrespective of socioeconomic class, to have access to kidney transplantation.' But the program is not just about recipients. The experience of Iran and the rest of the world has clearly shown that vendors are poor, hapless, jobless, indebted, and largely destitute. It is this social condition that compels the vendor to sell a kidney. The male–female ratio of 1.6 among Iranian vendors is in keeping with the published vendor demographics. It is exploitation of the poor that has enabled most Iranian kidney transplantations over the past two decades. Whether a vendor resides in Iran or is Pakistani or a Sudanese refugee or a Filipino, the fundamental unethical aspect is the same—it is a victimization of the poor.

Mahdavi-Mazdeh acknowledges that the Iranian model has, regrettably, provided little information about such a large nephrectomized patient population. She has carefully reviewed the literature to cite studies showing a less than 1% risk of kidney donors' developing end-stage renal disease, but none of these references is from an Iranian experience. Not cited is the reported health status of vendors from neighboring Pakistan. Many of these Pakistani vendors were bonded laborers, some jaundiced, some with inadequate kidney function, and some with stone

[1]*Department of Surgery, Harvard University, Boston, Massachusetts, USA*
Correspondence: *Francis L. Delmonico, Department of Surgery, Harvard University, 300 Longwood Avenue, Boston, Massachusetts 02115-5737, USA. E-mail: Francis_delmonico@neob.org*